

10/031,795

Page 3

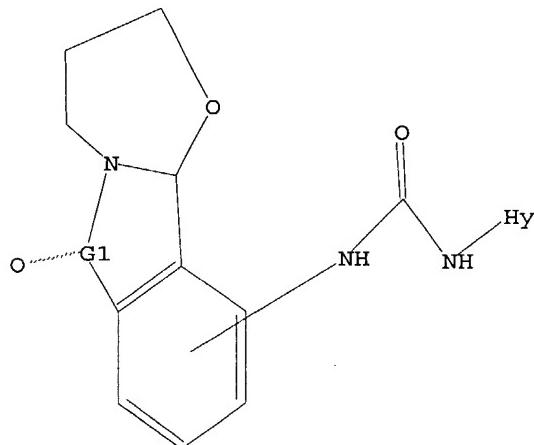
chain nodes :  
7 8 9 10 11 14  
ring nodes :  
1 2 3 4 5 6 13 15 16 17 18 19 20  
chain bonds :  
7-8 8-9 8-11 9-10 13-14  
ring bonds :  
1-2 1-6 2-3 3-4 3-13 4-5 4-16 5-6 13-15 15-16 15-20 16-17 17-18 18-19  
19-20  
exact/norm bonds :  
3-13 4-16 7-8 8-9 8-11 9-10 13-14 13-15 15-16 15-20 16-17 17-18 18-19  
19-20  
normalized bonds :  
1-2 1-6 2-3 3-4 4-5 5-6

G1:C,S

Match level :  
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom  
11:CLASS 12:CLASS 13:Atom 14:CLASS 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom  
20:Atom

L1 STRUCTURE UPLOADED

=> d 11  
L1 HAS NO ANSWERS  
L1 STR



G1 C,S

Structure attributes must be viewed using STN Express query preparation.

=> s 11  
SAMPLE SEARCH INITIATED 10:43:47 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

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Page 4

100.0% PROCESSED 1 ITERATIONS  
SEARCH TIME: 00.00.01 1 ANSWERS

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 1 TO 80  
PROJECTED ANSWERS: 1 TO 80

L2 1 SEA SSS SAM L1

=> s 11 sss full  
FULL SEARCH INITIATED 10:43:53 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 18 TO ITERATE

100.0% PROCESSED 18 ITERATIONS 18 ANSWERS  
SEARCH TIME: 00.00.01

L3 18 SEA SSS FUL L1

=> file caplus  
COST IN U.S. DOLLARS SINCE FILE TOTAL  
SESSION  
FULL ESTIMATED COST 155.42 155.63

FILE 'CAPLUS' ENTERED AT 10:43:58 ON 07 APR 2004  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
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FILE COVERS 1907 - 7 Apr 2004 VOL 140 ISS 15  
FILE LAST UPDATED: 6 Apr 2004 (20040406/ED)

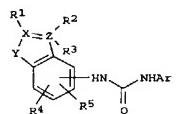
This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 13  
L4 2 L3

=> d ibib abs hitstr tot

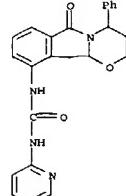
L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 2002:591913 CAPLUS  
 DOCUMENT NUMBER: 137:150215  
 TITLE: Cdk4 and/or Cdk6 inhibitors with biaryl ureas and their salts as antitumor agents  
 INVENTOR(S): Matayama, Satoshi; Hayashi, Kyoko; Honma, Mitsuki; Takahashi, Ikuko  
 PATENT ASSIGNEE(S): BANYU Pharmaceutical Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 194 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 200220338	A2	20020809	JP 2001-18755	20010126
PRIORITY APPLN. INFO.:			JP 2001-18755	20010126
OTHER SOURCE(S):	MARPAT	137:150215		
GI				



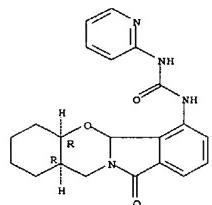
AB This invention relates to the general structures (I; Ar = N containing hetero aromatic ring, X, Z = C, etc.; Y = CO, etc.; R1-R5 = H, etc.) and their salts as Cdk4 and/or Cdk6 inhibitors. I have antiproliferative effects on cancer cells and are potential antitumor agents. Formulation examples of I capsules, tablets, and injections were given.  
 IT 322687-73-0 322687-74-1 322687-92-3  
 322688-08-0 322688-09-5 322688-26-6  
 322688-34-0 322688-35-7 322690-03-9  
 445431-55-1 445431-64-1 445431-68-5  
 445432-09-7  
 RL: (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Use)  
 (Cdk4 and/or Cdk6 inhibitors with biaryl ureas and their salts as antitumor agents)  
 RN 322687-73-0 CAPLUS  
 CN Urea, N-2-pyridinyl-N'-(3,4,6,10b-tetrahydro-6-oxo-4-phenyl-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 322687-74-1 CAPLUS  
 CN Urea, N-[(5aR,9aR)-4b,5a,6,8,9,9a,10,12-octahydro-12-oxo-7H-isoindolo[1,2-b][1,3]benzoxazin-4-yl]-N'-2-pyridinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 322687-92-3 CAPLUS  
 CN Urea, N-2-pyridinyl-N'-(3,4,6,10b-tetrahydro-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)

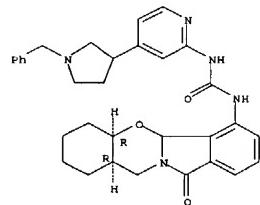
L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 322688-08-4 CAPLUS  
 CN Urea, N-[4-[1-(phenylmethyl)-3-pyrrolidinyl]-2-pyridinyl]-N'-(3,4,6,10b-tetrahydro-6-oxo-4-phenyl-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)

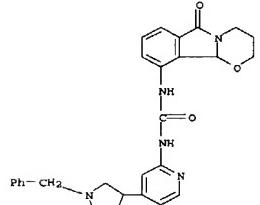
RN 322688-09-5 CAPLUS  
 CN Urea, N-[(Sax[9aR]-4b,5a,6,8,9,9a,10,12-octahydro-12-oxo-7H-isoindolo[1,2-b][1,3]benzoxazin-4-yl)-N'-(4-[1-(phenylmethyl)-3-pyrrolidinyl]-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



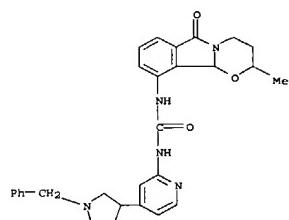
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 CN Urea, N-[4-[1-(phenylmethyl)-3-pyrrolidinyl]-2-pyridinyl]-N'-(3,4,6,10b-tetrahydro-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)



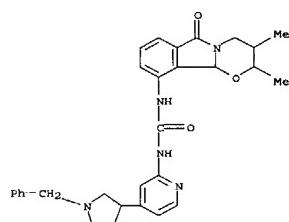
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L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

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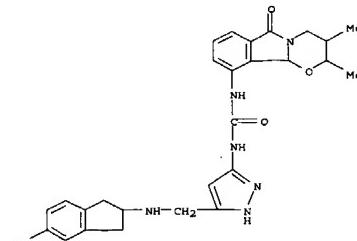
RN 322688-35-7 CAPLUS  
CN Urea, N-[4-(1-(phenylmethyl)-3-pyrrolidinyl)-2-pyridinyl]-N'-(3,4,6,10b-tetrahydro-2,3-dimethyl-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl]- (9CI) (CA INDEX NAME)



RN 322690-03-9 CAPLUS  
CN Urea,  
N-[5-[(5-bromo-2,3-dihydro-1H-inden-2-yl)amino]methyl]-1H-pyrazol-3-y]-N'-(3,4,6,10b-tetrahydro-2,3-dimethyl-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)

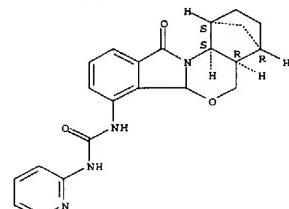
L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

(Continued)



RN 445431-59-4 CAPLUS  
CN Urea, N-[(1S,4R,4aR,12aS)-1,3,4,4a,5,6a,11,12a-octahydro-1,4-methano-2H-isoindolo[2,1-a][3,1]benzoxazin-7-yl]-N'-2-pyridinyl- (9CI) (CA INDEX NAME)

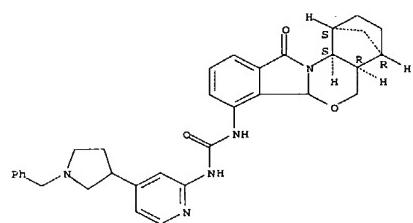
Absolute stereochemistry.



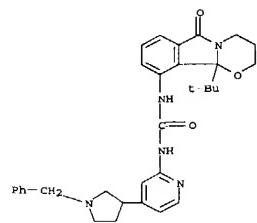
RN 445431-64-1 CAPLUS  
CN Urea, N-[(1S,4R,4aR,12aS)-1,3,4,4a,5,6a,11,12a-octahydro-1,4-methano-2H-isoindolo[2,1-a][3,1]benzoxazin-7-yl]-N'-(4-[1-(phenylmethyl)-3-pyrrolidinyl]-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

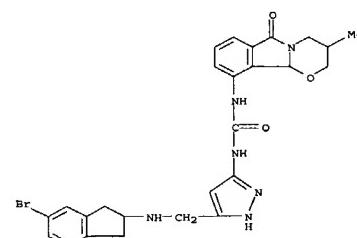


RN 445431-68-5 CAPLUS  
CN Urea, N-[10b-(1,1-dimethylethyl)-3,4,6,10b-tetrahydro-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl]-N'-(4-[1-(phenylmethyl)-3-pyrrolidinyl]-2-pyridinyl)- (9CI) (CA INDEX NAME)



RN 445432-09-7 CAPLUS  
CN Urea,  
N-[5-[(5-bromo-2,3-dihydro-1H-inden-2-yl)amino]methyl]-1H-pyrazol-3-y]-N'-(3,4,6,10b-tetrahydro-3-methyl-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



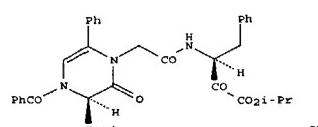
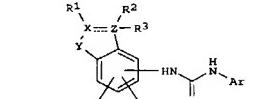
L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2001:78263 CAPLUS  
DOCUMENT NUMBER: 134:147614

TITLE: Preparation of N,N'-biarylurea derivatives as inhibitors of cyclin-dependent kinases (Cdk4 and Cdk6)  
INVENTOR(S): Hayama, Takeshi; Hayashi, Kyoko; Honma, Mitsutaka; Takahashi, Ikuiko  
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan  
SOURCE: PCT Int. Appl., 460 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001007411	A1	20010201	WO 2000-JP4991	20000726
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DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 2001106673	A2	20010417	JP 2000-274175	20000726
EP 1199306	A1	20020424	EP 2000-949909	20000726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
PRIORITY APPLN. INFO.: JP 1999-211384 A 19990726				
WO 2000-JP4991	W	20000726		

OTHER SOURCE(S): MARPAT 134:147614  
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L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

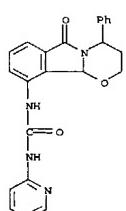


AB N-(hetero)aryl-N'-heterocyclylurea derivs. represented by general formula (I) [wherein Ar represents a nitrogenous heterocyclic aromatic group such as (un)substituted pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, thiazolyl, isothiazolyl, oxazolyl, isoquinazolyl, pyrazolyl, pyrrolyl, imidazolyl, indolyl, isoindolyl, quinolyl, isoquinolyl, benzothiazolyl or benzoxazolyl; X and Z each represents O or N taken together with R1 or R2 benzoate; CO = represents carbonyl, NH = represents NH-C(=O)-NH or NH-C(=O)-NH-Ar; R1 represents hydrogen, (un)substituted lower alkyl, Y3-W2-X4-R5, etc.; wherein R5 = H, (un)substituted lower alkyl, lower alkenyl, lower alkynyl, lower cycloalkyl, aryl, imidazolyl, isoquinazolyl, isoindolyl, indazolyl, indolyl, indolidinyl, isothiazolyl, ethylenedioxypyrenyl, oxazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, pyrazolyl, quinoxalinyl, quinolyl, etc.; W2 = single bond, O, S, SO, SO2, N-(un)substituted NH, SO2NH, NHSO2NH, NHSCO2, CONH, NHCO, NHCO2, etc.; Y3, Y4 = single bond, linear or branched lower alkylene; R2 and R3 each represents hydrogen, lower alkyl or alkoxy, or Y3-W2-Y4-R5 (Y3, W2, Y4, R5 = same as above), or one of R2 and R3 together with Y3 and X forms cyclohexane, cyclopentane, piperidine, 4,5-dihydro-1,3-diazole, tetrahydrothiophene, pyrrolidine, tetrahydropyran, tetrahydro-1,3-diazepine, tetrahydro-1,3-diazoline, tetrahydro-1,3-diazepine, tetrahydro-1,3-diazepine, tetrahydro-1,3-diazepine, tetracyclic, etc.; R6 = H, halo, amino, or Y3-W2-Y4-R5 (Y3, W2, Y4, R5 = same as above) or salts thereof are prepared. The compds. (e.g., II) have a remarkable proliferation-inhibitory effect on tumor cells. A Cdk4 and/or Cdk6 inhibitor for use in the therapy of malignant tumor can hence be provided. II showed IC50 of 0.061 and 0.019 μM against cyclin-D1-Cdk4 and cyclin-D2-Cdk4, resp., vs. 0.36 and 0.056 μM, resp., for (z)-flavopiridol, and inhibited the proliferation of HCT116 and MKN-1 cells with IC50 of 0.013 and 0.10 μM, resp., vs. 0.15 and 0.87 μM, resp., for (z)-flavopiridol. Pharmaceutical formulations containing I were prepared]

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

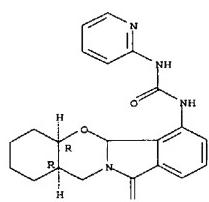
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322688-29-9P 322688-34-6P 322688-35-7P  
322690-03-9P 322690-04-OP  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses); (preparation of N-(hetero)aryl-N'-heterocyclylurea derivs. as in inhibitors of cyclin-dependent kinases (Cdk4 and Cdk6) and antitumor agents)

RN 322687-73-0 CAPLUS  
CN Urea, N-2-pyridinyl-N'-(3,4,6,10b-tetrahydro-6-oxo-4-phenyl-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)



RN 322687-74-1 CAPLUS  
CN Urea, N-2-pyridinyl-N'-(3,4,6,10b-tetrahydro-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)

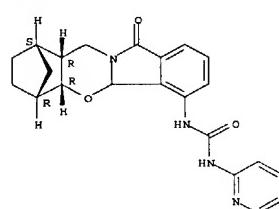
Absolute stereochemistry.



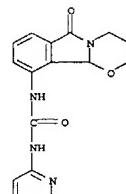
L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 322687-75-2 CAPLUS  
CN Urea, N-[(5aR,6R,9aR)-4b,5a,6,8,9,9a,10,12-octahydro-6-oxo-2H-[1,3]benzoxazin-4-yl]-N'-2-pyridinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



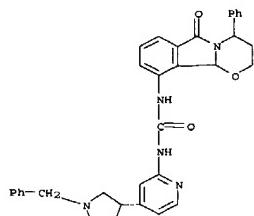
RN 322687-92-3 CAPLUS  
CN Urea, N-2-pyridinyl-N'-(3,4,6,10b-tetrahydro-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)



RN 322688-08-4 CAPLUS  
CN Urea, N-[(4-[(1-phenylmethyl)-3-pyrrolidinyl]-2-pyridinyl)-N'-(3,4,6,10b-tetrahydro-6-oxo-4-phenyl-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

(Continued)



RN 322688-09-5 CAPLUS

CN Urea, N-[{(5aR,9aR)-4b,5a,6,8,9,9a,10,12-octahydro-12-oxo-7H-isoindolo[1,2-b][1,3]benzoxazin-4-yl]-N'-(1-(phenylmethyl)-3-pyrrolidinyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Chemical structure showing a benzimidazole ring fused to a pyrrolidine ring, which is further substituted with a phenyl group and a cyclohexane ring.

RN 322688-10-8 CAPLUS

CN Urea, N-[{(5aR,6,9S,9aR)-4b,5a,6,8,9,9a,10,12-octahydro-12-oxo-6,9-methano-7H isoindolo[1,2-b][1,3]benzoxazin-4-yl]-N'-(3-(1-(phenylmethyl)-2-pyrrolidinyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

(Continued)

Chemical structure showing a benzimidazole ring fused to a pyrrolidine ring, which is further substituted with a phenyl group and a cyclohexane ring.

RN 322688-29-9 CAPLUS

CN Urea, N-2-pyridinyl-N'-(3,4,6,10b-tetrahydro-2,3-dimethyl-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)

Chemical structure showing a benzimidazole ring fused to a pyrrolidine ring, which is further substituted with a phenyl group and a cyclohexane ring.

RN 322688-34-6 CAPLUS

CN Urea, N-[4-(1-(phenylmethyl)-3-pyrrolidinyl)-2-pyridinyl]-N'-(3,4,6,10b-tetrahydro-2-methyl-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)

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L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

(Continued)

Chemical structure showing a benzimidazole ring fused to a pyrrolidine ring, which is further substituted with a phenyl group and a cyclohexane ring.

RN 322688-26-6 CAPLUS

CN Urea, N-[4-(1-(phenylmethyl)-3-pyrrolidinyl)-2-pyridinyl]-N'-(3,4,6,10b-tetrahydro-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)

Chemical structure showing a benzimidazole ring fused to a pyrrolidine ring, which is further substituted with a phenyl group and a cyclohexane ring.

RN 322688-28-8 CAPLUS

CN Urea, N-2-pyridinyl-N'-(3,4,6,10b-tetrahydro-2-methyl-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

(Continued)

Chemical structure showing a benzimidazole ring fused to a pyrrolidine ring, which is further substituted with a phenyl group and a cyclohexane ring.

RN 322688-35-7 CAPLUS

CN Urea, N-[4-(1-(phenylmethyl)-3-pyrrolidinyl)-2-pyridinyl]-N'-(3,4,6,10b-tetrahydro-2,3-dimethyl-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)

Chemical structure showing a benzimidazole ring fused to a pyrrolidine ring, which is further substituted with a phenyl group and a cyclohexane ring.

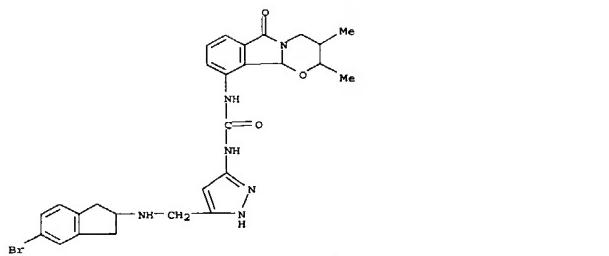
RN 322690-03-9 CAPLUS

CN Urea, N-[5-((5-bromo-2,3-dihydro-1H-inden-2-yl)aminomethyl)-1H-pyrazol-3-yl]-N'-(3,4,6,10b-tetrahydro-2,3-dimethyl-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)

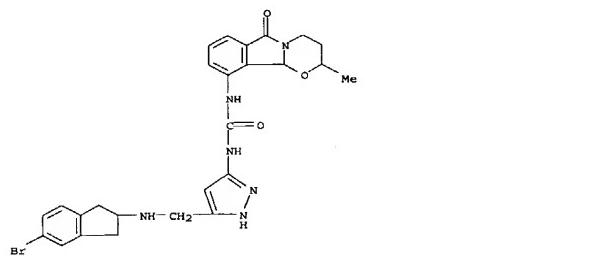
04/07/2004

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

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RN 322690-04-0 CAPLUS  
 CN Urea,  
 N-[5-[(5-bromo-2,3-dihydro-1H-inden-2-yl)amino]methyl]-1H-pyrazol-3-  
 yl]-N'-(3,4,6,10b-tetrahydro-2-methyl-6 oxo-2H-[1,3]oxazino[2,3-a]isoindol-  
 10-yl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR  
 THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT